

The University of Chicago

EVALUATION OF THE KUHN EFFECT

A PART OF A DISSERTATION SUBMITTED TO
THE FACULTY OF THE DIVISION OF THE
PHYSICAL SCIENCES IN CANDIDACY FOR
THE DEGREE OF DOCTOR OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY

1935

By

JOSEPH A. CHENICEK

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NOTE

Reproduced here is Part I of a dissertation entitled
"I. Evaluation of the Kuhn Effect. II. The Determination of the
Structure of the Condensation Product of an Aldehyde, β -Naphthol
and Ammonia."

The author wishes to express his appreciation to Profes-
sor M. S. Kharasch and to Dr. J. K. Senior for their valuable ad-
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I. EVALUATION OF THE KUHN EFFECT

The purpose of the present investigation is probably best explained by a review of the work which led up to it.

It had been found by many investigators that if an optically active base is combined successively with a number of optically inactive acids, the dilute equimolecular aqueous solutions of the resulting salts have nearly identical rotations. A similar uniformity of rotation is found in the dilute solutions of the salts formed by the union of a given optically active acid with a variety of optically inactive bases. Hädrich¹ explained these findings on the basis of the dissociation hypothesis. The salts mentioned should, under the stated conditions, be almost completely dissociated, and their equimolecular solutions should contain nearly equal amounts of the single optically active ion. On the usual assumption that the effect of ions on the properties of solutions is additive, the optical rotation of such dilute salt solutions should be independent of the inactive ion. Hence there is a certain rotation characteristic of each optically active ion in dilute solution. This rotation may be called "normal." If the rotation of any particular salt containing only one optically active ion deviates widely from the normal, the divergent rotation may be called "anomalous."

Hädrich showed that the work of Oudemans² permitted the extension of the above hypothesis to certain non-aqueous solutions.

¹Hädrich, Zeit. physik. Chem., 12, 476 (1893).

²Oudemans, Rec. trav. chim., 1, 48 (1882).

In 1927 Kuhn and Albrecht¹ found that in alcohol the rotations of quinine m-nitrobenzoate and phthalate correspond closely to that of the free alkaloid (-164° to -168°). This rotation they assumed to be the normal one for the quinonium ion. On the other hand quinine 4,4'-dinitrodiphenate in alcohol or in chloroform is strongly dextrorotatory -- that is, it exhibits a marked anomaly in rotation.

In 1932 Kuhn² attempted to explain this anomaly by assuming the existence of labile enantiomorphous forms of the acid ion. It is known that certain diphenyl derivatives can be resolved into optical antipodes. The theory in regard to these substances is as follows: If substituents are introduced into the phenyl rings of diphenyl in such a way that neither ring retains its plane of symmetry and the two are prevented from occupying a coplanar position, then the molecule has no element of reflection symmetry and should be optically active.



Presumably steric hindrance between the substituents ortho to the interannular bond is what prevents the rings from attaining a coplanar configuration. If the ortho substituents are small enough the free rotation of the phenyl groups is not hindered, and there should be no optical activity. Thus diphenic acid has not been resolved because the two ortho hydrogens are too small to restrict free rotation.

¹Kuhn and Albrecht, Ann., 455, 272 (1927).

²Kuhn, Ber., 65B, 49 (1932).

Kuhn supposed that in quinine 4,4'-dinitrodiphenate the dissymmetric quinonium ion threw the phenyl rings of the acid ion out of the coplanar position and produced an excess of one antipode. The dissymmetry thus introduced into the acid ion would account for the anomalous rotation of the salt. However when the acid was recovered, it was found to be inactive, and so Kuhn concluded that the dissymmetry of the acid ion persisted only in the presence of the optically active base.

Previous to this work of Kuhn, there had been found a number of optically active substances which exhibited the following behavior: When a suitable optically active agent was added to a 50-50 mixture of their antipodes, the entire substance was precipitated as one optically active form. When the dissymmetric agent was removed this form slowly racemized -- a process marked by the mutarotation of its solution. The name "asymmetric rearrangement" had been applied to the phenomenon described.

Kuhn proposed to divide the cases of asymmetric rearrangement into two classes:

1. Where the optical activity persisted (at least in part) after the removal of the activating agent, and the autoracemization could be observed as a mutarotation, he suggested the term "asymmetric rearrangement of the second type."
2. Where the optical activity vanished with the removal of the activating agent -- that is, where the autoracemization was too rapid to be observed, he suggested the term "asymmetric rearrangement of the first type." The behavior of 4,4'-dinitrodiphenic acid in the presence of quinine he regarded as an instance of this first type.

As other examples of the same type Kuhn cited certain salts described by Quehl and Pfeiffer.¹ These compounds have the general formula $Zn(R)_3 X_2$ where R occupies two coordination spaces about the zinc atom and X is a dissymmetric univalent ion. When R was α -phenanthroline or α, α -dipyridyl, Quehl and Pfeiffer could not resolve the base into antipodal forms, but the solutions of the salts showed rotations markedly different from the simple zinc salts of the corresponding acids. For example, zinc bromocamphorsulphonate showed a rotation of -4.55° but when three mols of α -phenanthroline were added the rotation changed to -8.44° . Quehl and Pfeiffer also suggested that dissymmetry was induced into the complex base by the optically active acid.

Recently Lesslie and Turner² have made a number of observations on diphenic acid itself. They found that in alcohol-chloroform solutions the diphenates of quinine and cinchonidine are strongly dextrorotatory, although the inorganic salts of these bases show a laevorotation. To explain this anomaly they used Kuhn's hypothesis. They also observed a slight mutarotation (the rotation always increasing with time) in alcohol and alcohol-chloroform solutions but not in chloroform alone. This mutarotation they explained by assuming that when the diphenic acid is added to certain solutions of quinine there occurs a very rapid asymmetric induction, only the last stages of which are detectable with the polariscope.

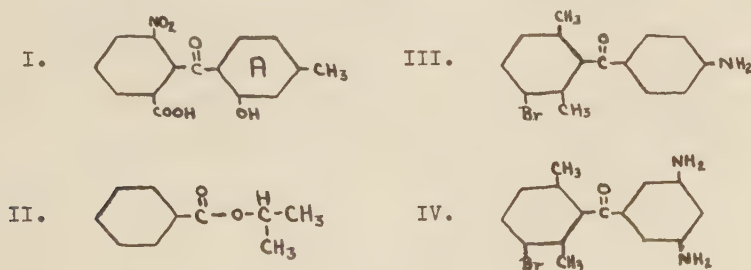
Lesslie and Turner also observed the rotation of quinine diphenate at different concentrations. According to the theory of asymmetric induction, the dextrorotation of a solution of quinine diphenate should increase with percentage of undissociated

¹Quehl and Pfeiffer, Ber., **65B**, 560 (1932).

²Lesslie and Turner, J. Chem. Soc., pp. 347 (1934).

salt present. This conclusion was supported by experiment, for, at higher concentrations the rotation was larger than at smaller concentrations. Similarly by increasing ionization the induced dissymmetry should be decreased. In aqueous alcohol, therefore, the rotation of quinine diphenate should be less positive, the greater the percentage of water present. Again the results supported the assumption.

Adams¹ observed several anomalous rotations but did not attach particular significance to them. He found that the brucine salt of 2-(2-hydroxy-4-methyl-benzoyl)-3-nitrobenzoic acid (I) has a rotation of 18.3° , although brucine itself has a rotation of -119° and brucine hydrochloride one of -84° . The free acid recovered from the salt was, however, optically inactive. When the phenyl group (A) in (I) was replaced by an aliphatic group (II) normal rotation resulted. The anomaly also disappeared when one of the ortho substituents was removed (III and IV).



To the Kuhn hypothesis, Adams raises objections based upon results obtained by himself and other investigators. Several workers call attention to anomalies in the rotation of salts and esters.² Hilditch³ and Rupe⁴ point out that an anomaly in

¹Adams, J. Am. Chem. Soc., 50, 2499 (1928).

²Walden, Zeit. physik. Chem., 20, 569 (1896).

³Hilditch, J. Chem. Soc., 93, 1 (1908).

⁴Rupe, Trans. Far. Soc., X, 46 (1914).

rotating power always accompanies the presence of a conjugated system close to the carbonyl group. Rupe further shows that whenever conjugation is destroyed by reducing a double bond or a benzene nucleus, the strong effect upon rotation vanishes.

If the Kuhn hypothesis is valid then isomer numbers can be determined from anomalies in the optical rotations of salts. Hence before accepting so radical a departure from classic chemical practice it is desirable to determine the validity of the Kuhn idea. The purpose of the present investigation is in fact two fold.

1. To test the validity of the Kuhn hypothesis.
2. In case this hypothesis should prove untenable, to attempt to determine the cause of the anomalous rotations of certain quinine salts.

To attain the first of these objects the rotations of a large number of quinine salts in chloroform were taken in order to determine whether quinine 4,4'-dinitrodiphenate really does have an anomalous rotation and whether other acids which probably cannot be dissymmetrized also produce similar anomalies. Since Oudemans¹ had found that all quinine salts in water solution show the same rotation when treated with excess acid, it was thought that perhaps all of the organic salts of quinine including the dinitrodiphenate would have the same rotation when a large excess of the acid was present.

Procedure.--Individual samples containing one mol of optically active base to varying amounts of acid (from one-fourth to twenty mols) were weighed out in 25 cc. volumetric flasks. Then the mixture of base and acid was dissolved in pure dry chloroform. The solution was brought to 20° C. in a thermostat, poured

¹See page 11.

into a water-jacketed 2 dcm. polariscope tube and the rotation taken at 20° C. The green line of mercury (5461 Å) was used.¹ The results were plotted with equivalent acid/mols base as the abscissa and $\alpha_{5461}^{20^\circ}$ (rotation of a 2 dcm. tube of the salt) as the ordinate.

Results.--The results are summarized in the following graphs (pp. 14-18).

Figure 1. Quinine and aliphatic acids in chloroform.

Figure 2. Quinine and phenyl-substituted aliphatic acids in chloroform.

Figure 3. Quinine and ortho-substituted benzoic acids in chloroform.

Figure 4. Meta-, para-, di-, and tri-substituted benzoic acids with quinine in chloroform.

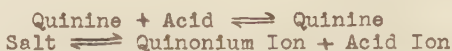
Figure 5. Quinine with dibasic acids in chloroform.

For the actual rotations obtained see Experimental Part.

Discussion of the results.--The curves obtained by plotting the change of rotation of quinine with increasing amounts of acids are of such diversified character that no one of them can be called normal or anomalous. Moreover, if the rotation of the 4,4'-dinitrodiphenate is assumed to be anomalous then the rotations of the 2,4-dinitrobenzoate and the 2,4,6-trinitrobenzoate must also be anomalous since they give approximately the same curves as the dinitrodiphenate. It follows according to the Kuhn theory, that these nitrobenzoic acids can undergo "asymmetric rearrangement of the first type." Since it is highly improbable that they can exist as pairs of optical antipodes, there is no basis for Kuhn's theory that 4,4'-dinitrodiphenic acid is dissymmetrized in the presence of quinine.

¹The D line of sodium (5893 Å) gave similar results.

It is also evident from the curves that all of the quinine salts do not have the same optical rotation when an excess of acid is present, as might be expected from the work of Oudemans. According to Oudemans after a certain concentration is reached, the rotations of salts should be equal. Instead, the curves diverge widely and show marked peculiarities. For example, many of the curves have a minimum where the molar ratio of acid to base is one. The occurrence of this minimum should be accounted for if possible. It may, perhaps, be explained by the following equilibrium:



When acid is added to one mol of quinine the salt should form as an approximately linear function of the amount of acid until about one equivalent of the acid is present. At this point the highest concentration of ionized salt is present since, if more acid is added the equilibrium will shift toward the unionized salt. This point would be represented by the minimum of the curve. Then, as the ionization is repressed by the addition of acid the rotation changes until the greatest possible amount of unionized salt is formed. This amount would depend upon the ionization of the salt in chloroform solution. Unfortunately no data are available to determine this point.

Other interesting facts also appear when the curves are examined. All of the aliphatic acids give curves of the same general shape, with no minimum, while aromatic acids give curves which can be divided into two classes:

1. Curves for the salts of o-substituted benzoic acids which show no minimum but which show continuous increase in laevorotation with increase in acid.

2. Curves for the salts of o- and p-substituted benzoic acids which show a minimum.

The ortho-substituted benzoic acids with negative groups like NH_2 , Cl, Br, I, or OH give curves without a minimum while those with positive substituents like COOH and NO_2 and all p-benzoic acids give curves with a minimum.

Determination of the Factors Influencing Rotation

Since, during the investigation of the Kuhn effect, it became apparent that the amount of the rotation of quinine salts is a very complicated matter, it was decided to attempt an evaluation of the influences on which this amount depends. In general the rotation of a given optically active compound is influenced by the following variables:

1. Length of tube
2. Temperature
3. Wave-length of light
4. Concentration
5. Solvent

The first four of these are easily controlled so that standard conditions for investigating the solvent effect can be readily obtained. In spite of the vast amount of work that has been done on this effect, the influence of the solvent on rotation is not yet clearly understood. It is well known that a substance may be laevorotatory in one solvent and dextrorotatory in another. Rule¹ has published many papers on the influence of solvents and has concluded that the rotation of the solute varies with the dipole of the solvent. In solvents derived from benzene the higher the dipole of the solvent the lower the rotation. He

¹Rule, J. Chem. Soc., pp. 674 (1931); pp. 1409 (1932).

asserts that the rotatory power most characteristic of an optically active solute is exhibited when it is dissolved in a non-polar solvent such as carbon tetrachloride or benzene. Recently he has announced that the rotation of d-pinane in various solvents is chiefly governed by the refractive index of the solvent medium.¹

Many investigators have discussed the possibility that association of the solute in certain solvents may account for the abnormalities in rotation;^{2,3} but, in general, there does not seem to be much connection between association and rotation. Patterson⁴ determined rotation dispersion curves for certain substances in solution under widely varying conditions. He found that the curves for a single substance differed only slightly and concluded that association, dissociation, solvation, dynamic isomerism and residual affinity were either non-existent or had unimportant effects on optical rotation.

The influence of dissociation has been discussed by other workers. The hypothesis of Hädrich has already been explained. He supported his opinion by showing that, when an alkaloid is neutralized by different acids and the solutions are treated with increasing amounts of water, (1) the molecular rotations after reaching a certain concentration become constant, and (2), that the constant values for the rotations of the different salts are nearly the same.

¹Rule and Chambers, Nature, 133, 910 (1934).

²Freundler, Ann. chim. phys., (7) 4, 256 (1895).

³Patterson, J. Chem. Soc., pp. 167 (1901).

⁴Ibid., pp. 1176 (1916).

Biddle and Watson¹ found that the rotations of cinchonine, cinchonidine, and cinchotoxine salts are directly proportional to the concentration of the active bivalent ion. Hadrich's results were thus confirmed.

If the dissociation of an optically active compound is diminished by adding other electrolytes to the solution a change in rotatory power follows. Oudemans² noticed this effect when he treated diacid alkaloids with 1, 2 and up to 80 mols of different acids in aqueous solution. The specific rotation first increased to a maximum which appeared when somewhat more acid was present than was required for the formation of the neutral salt; then a continuous small decrease took place. Tykociner³ also noticed the same effect when he added excess acid to brucine, strychnine, morphine, and codeine.

Oudemans drew the following conclusions from his research:

1. The optical activities of the aqueous solutions of neutral salts of an active mono-acid base are identical and independent of the chemical character of the inactive acid with which the base is united. The small differences are the result of partial and unequal decompositions of these salts.

2. Where the neutral salt is not decomposed by water, excess acid does not affect the rotation. The small deviation sometimes observed between the maximum value and the value for the neutral salt is the result of partial decomposition.

3. The diacid bases form two series of salts. Each of these series has a characteristic optical rotation, usually much smaller for the basic salts than for the neutral salts.

¹Biddle and Watson, J. Am. Chem. Soc., 39, 968 (1917).

²Oudemans, op. cit., 1, 18 (1882).

³Tykociner, ibid., 6, 144 (1884).

Recently Lesslie and Turner¹ added successive quantities of diphenic acid to an alcohol-chloroform solution of quinine. The laevorotation decreased as a linear function of the amount of acid until 0.4 of a mol of the latter per mol of base was present. Thereafter it fell to a constant value at about 1.5 mols.

Cohen² has done a great deal of work on the rotations of menthyl benzoate and its substitution derivatives. He found that when substituents are introduced into the ortho-position a large change in rotation occurs, but that when the meta- and para-positions are substituted practically no effect is noticeable. Rule³ has found that in these menthyl esters the influence of the ortho-substituents on rotation is similar to their effect on the molecular inductive capacity and follows their order in the polar series as deduced from the nitration of the correspondingly substituted benzenes. He believes that the position of the group in the polar series and its proximity to the asymmetric center are the factors which govern the effect of a substituent group on rotation.

Results.--

Figure 1. Aliphatic acids with quinine in chloroform.

Figure 2. Phenyl-substituted aliphatic acids with quinine in chloroform.

Figure 3. Ortho-substituted benzoic acids with quinine in chloroform.

Figure 4. Meta-, para-, di-, and tri-substituted benzoic acids with quinine in chloroform.

¹Cohen, J. Chem. Soc. (series appearing during years 1905 to 1908 inclusive).

²Lesslie and Turner, op. cit., pp. 347 (1934).

³Rule, op. cit., pp. 2188 (1925).

Figure 5. Dibasic acids with quinine in chloroform.

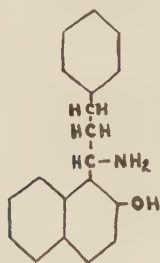
Figure 6. Acids with quinine in cellosolve (ethylene glycol monoethyl ether).

Figure 7. Acids with hydroquinine and quininechloride in chloroform.

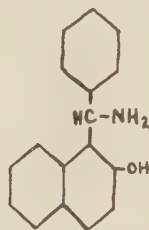
Figure 8. Acids with benzoyl- and acetylquinine in chloroform.

Figure 9. Acids with brucine in chloroform.

Figure 10. Acids with morphine, Howard's and Betti's base in cellosolve.

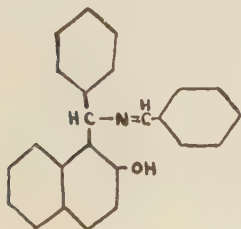


Howard's base

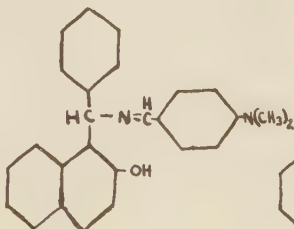


Betti's base

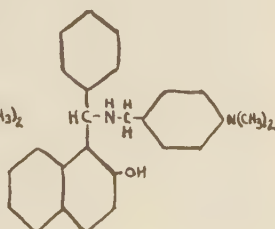
Included in the Experimental Part are the results for acids with d- Betti's Schiff base (I), d-p-dimethylaminobenzal-β-naphtholphenylaminomethane (II), and d-p-dimethylaminobenzyl-β-naphtholphenylaminomethane (III) in chloroform.



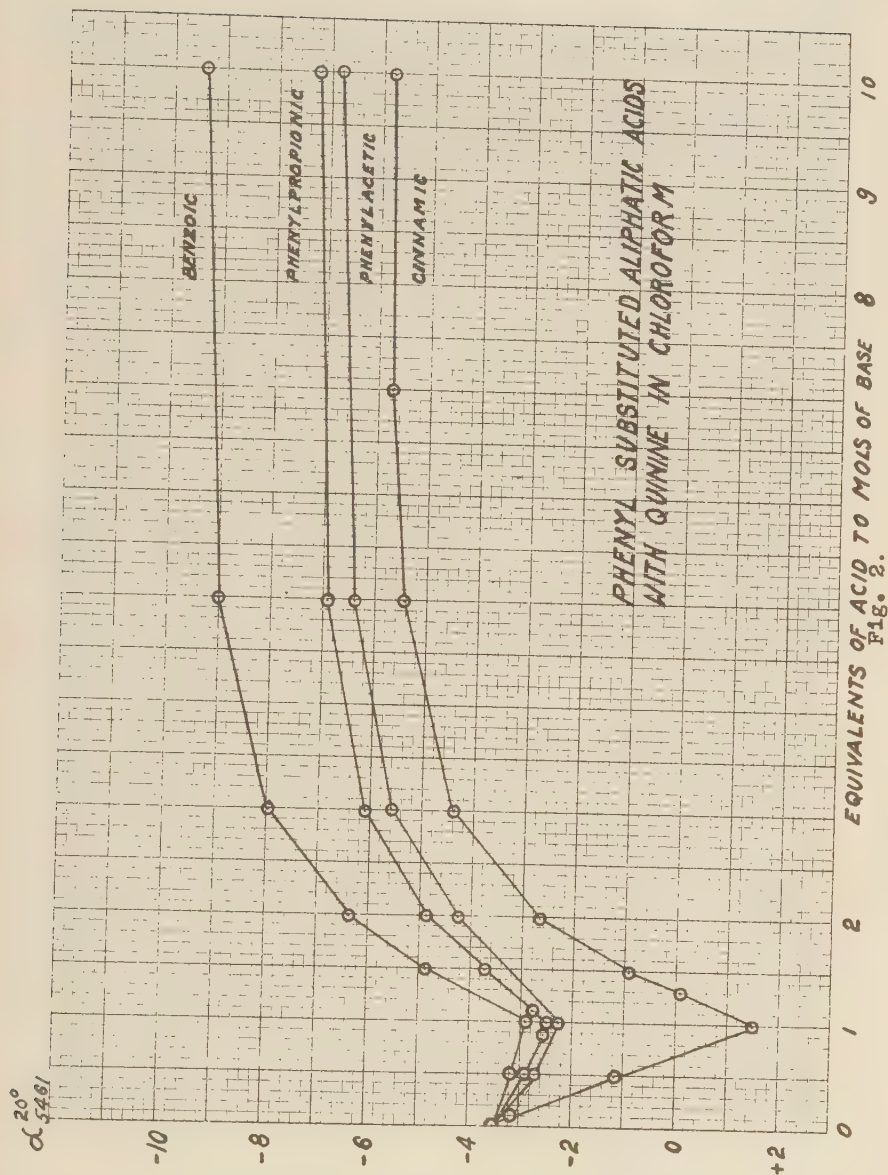
I.



II.



III.



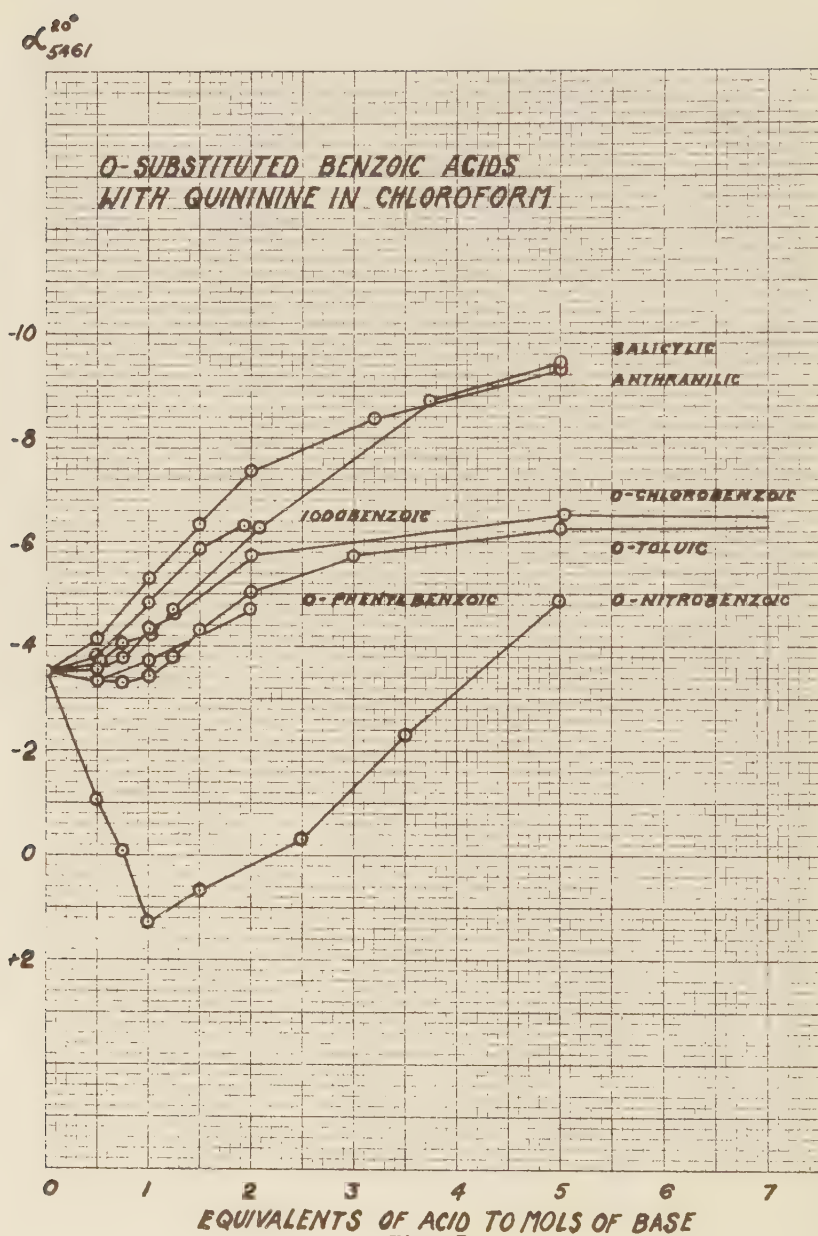


Fig. 3.

α^{20°
5481

M- AND P-MONOSUBSTITUTED AND DI- AND TRI-SUBSTITUTED BENZOIC ACIDS WITH QUININE IN CHLOROFORM

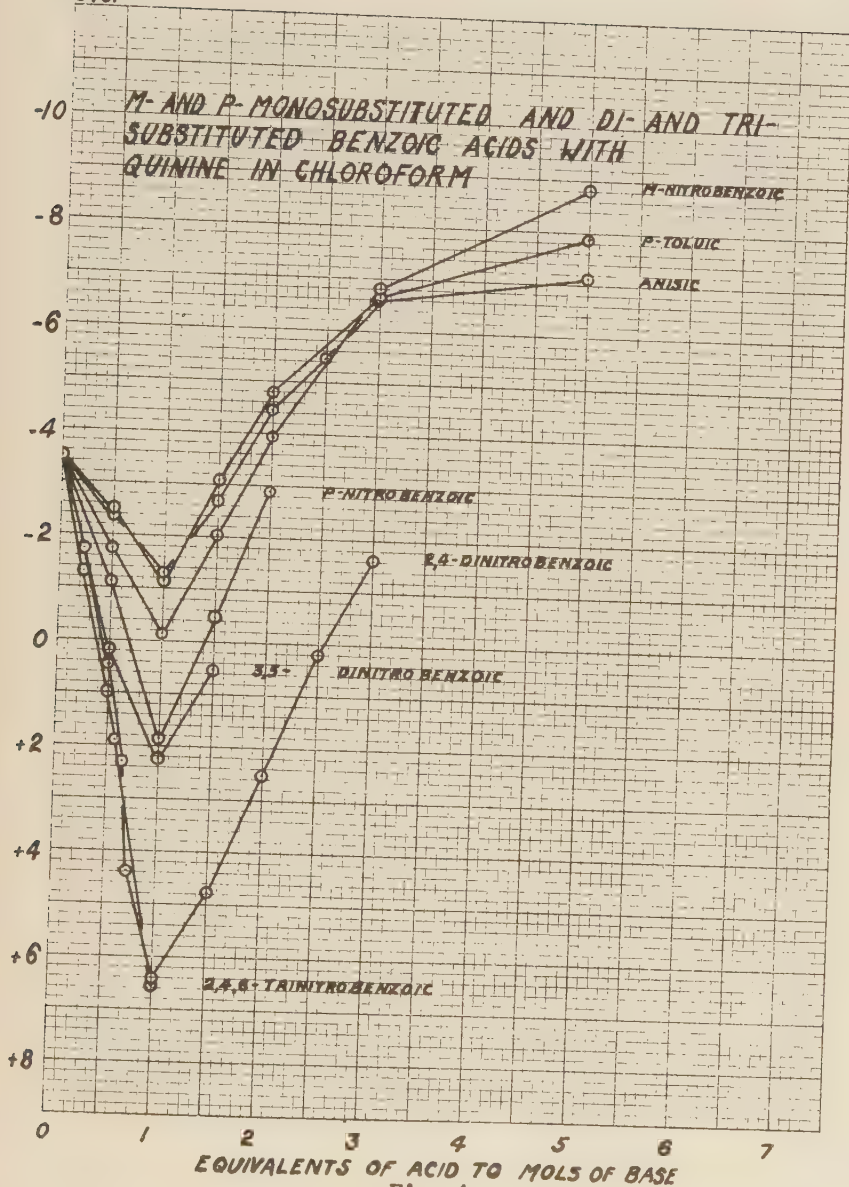
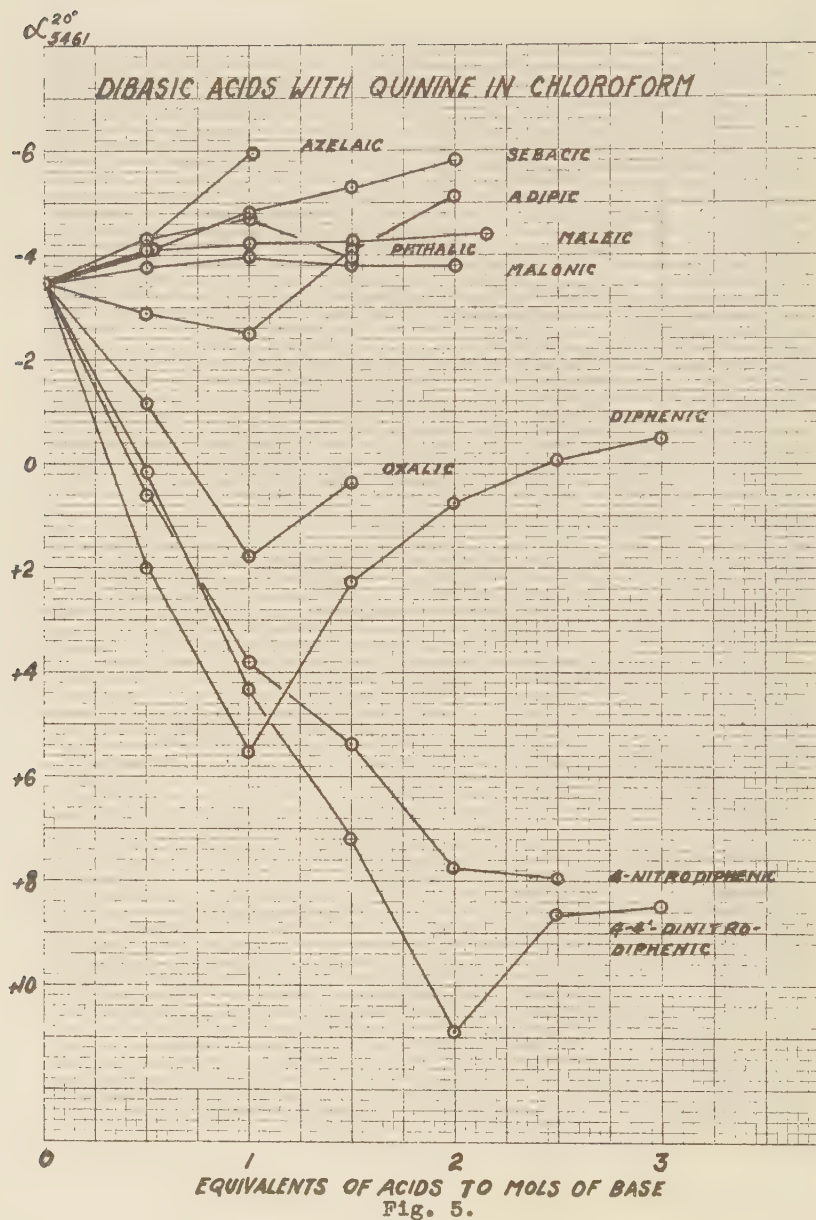
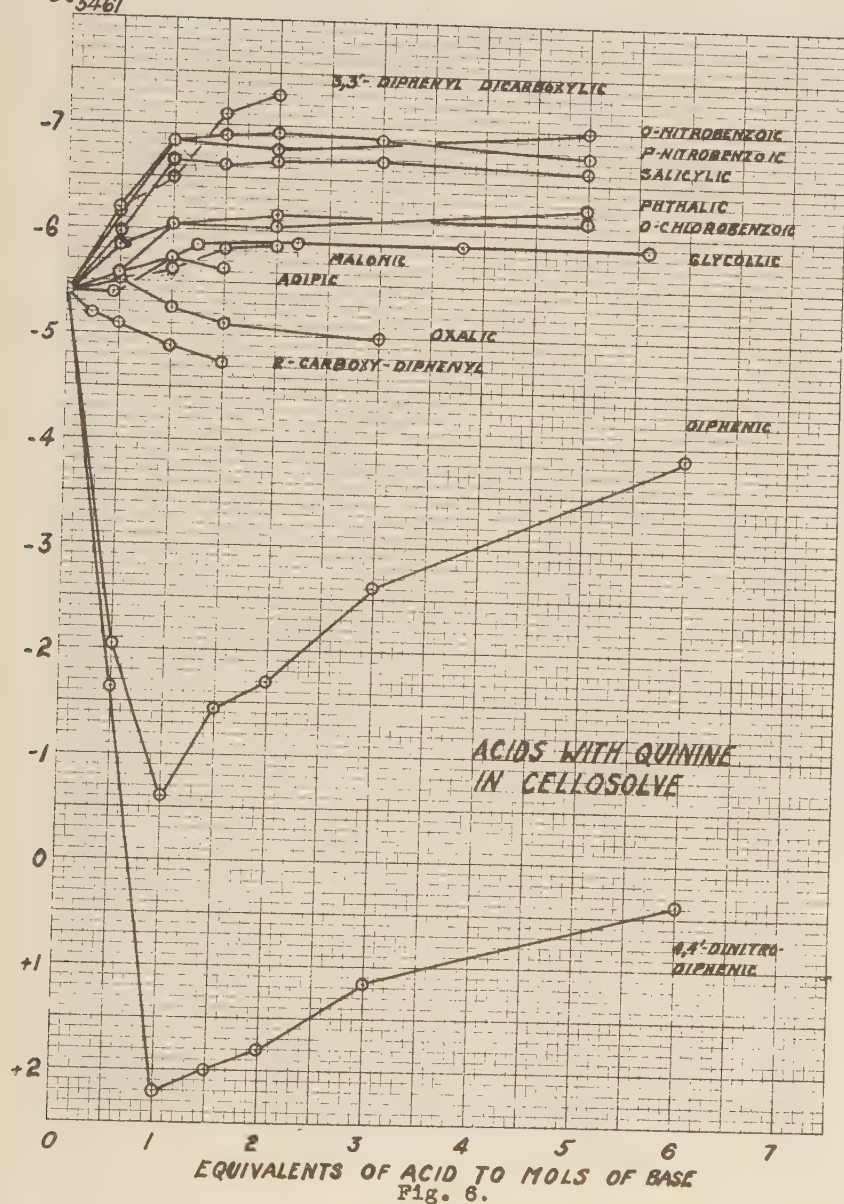
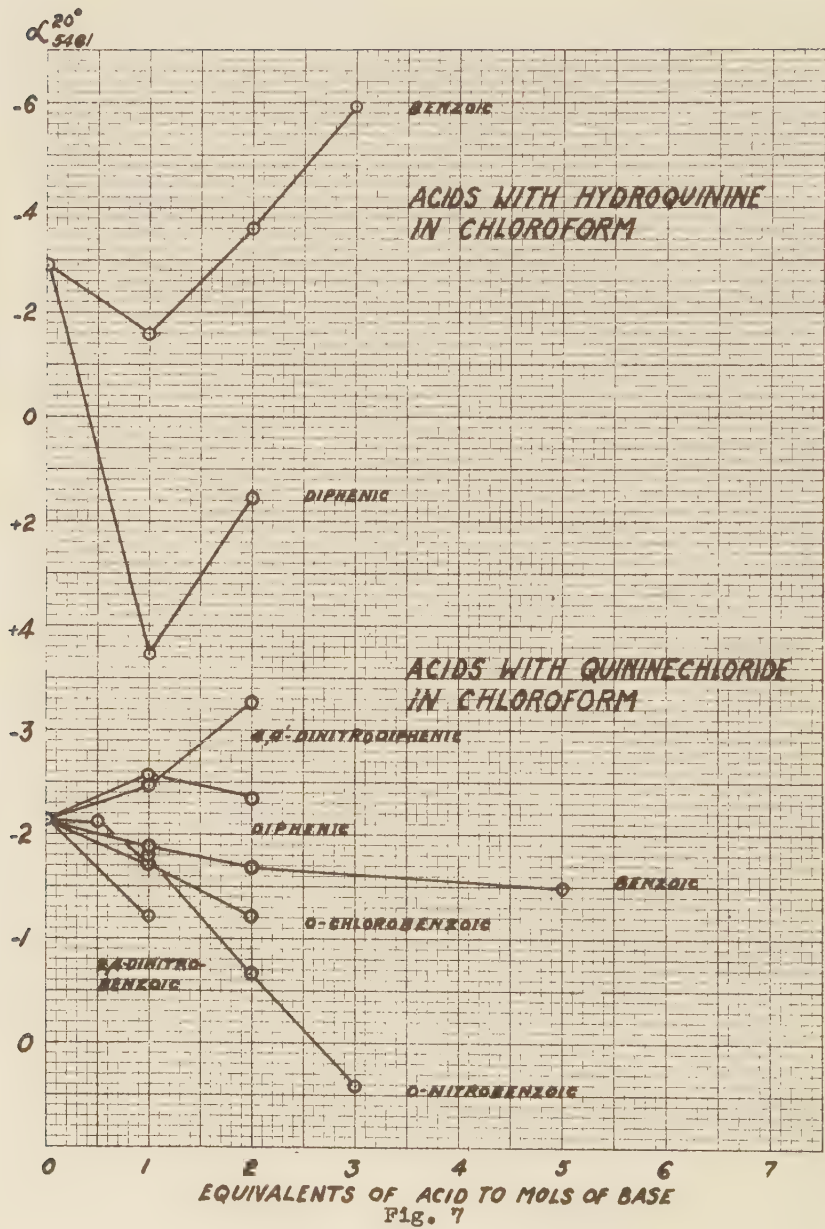


Fig. 4.



α^{20}
5461





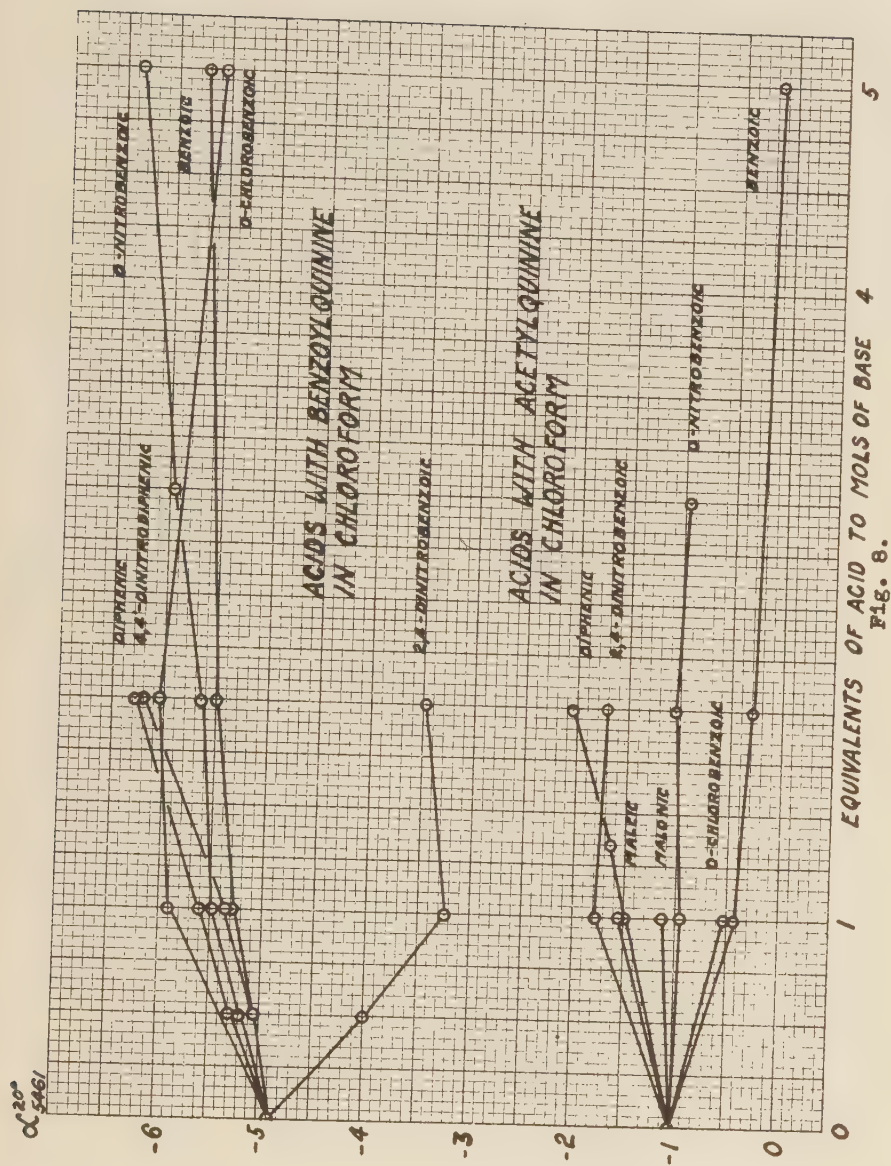


Fig. 8.

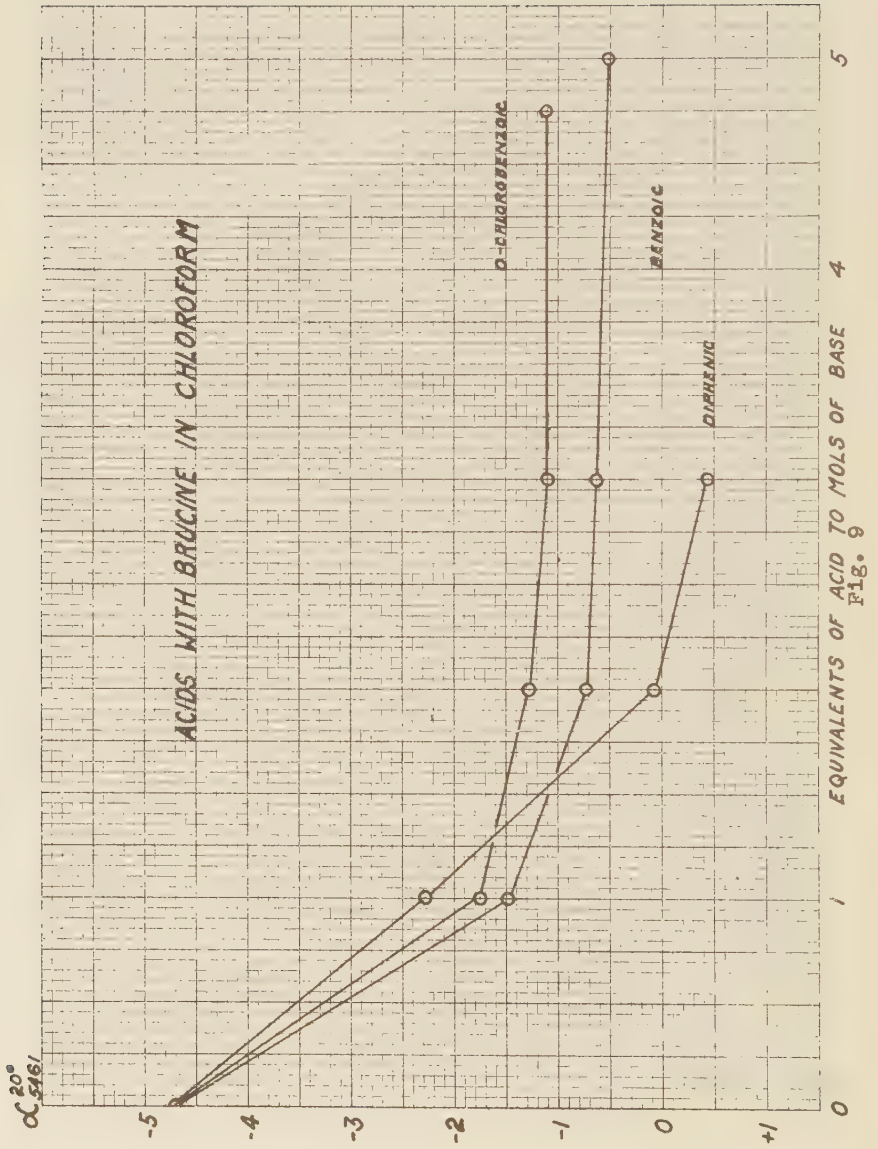


Fig. 9

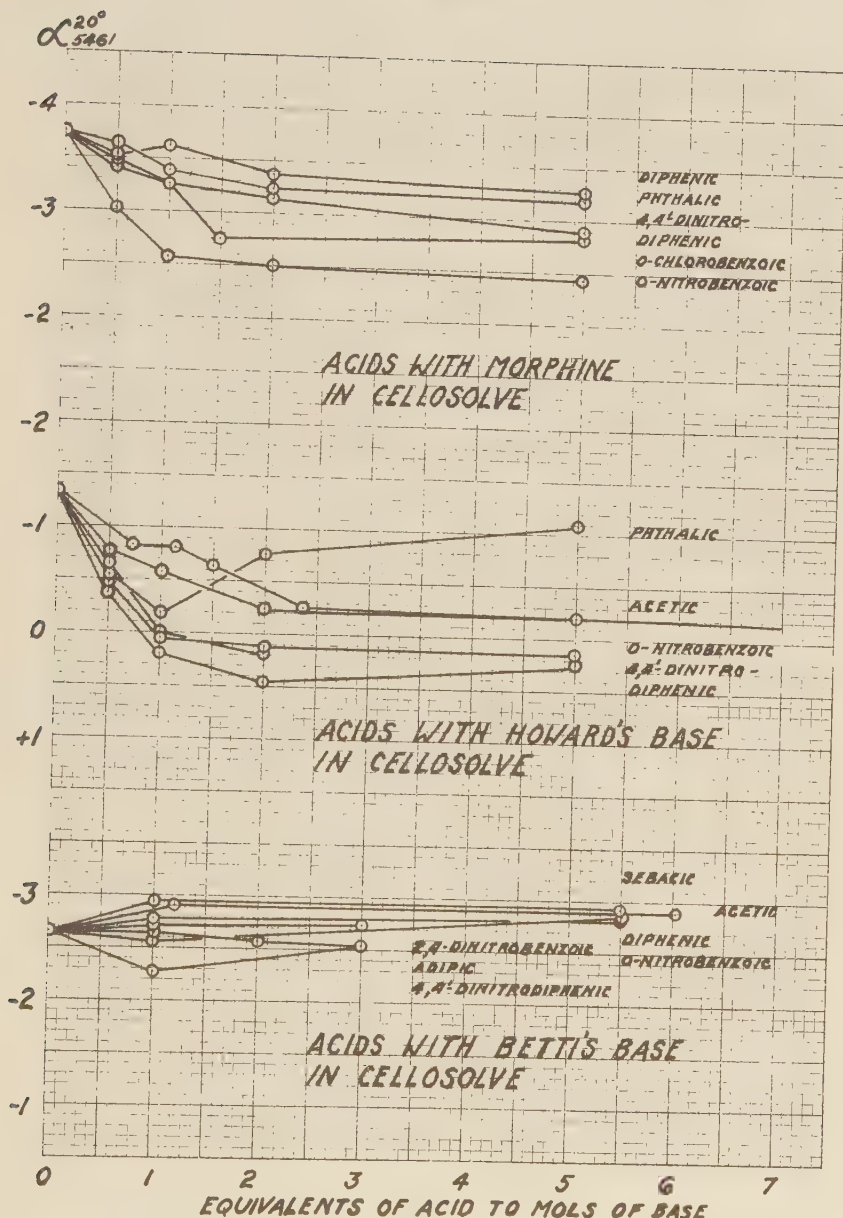


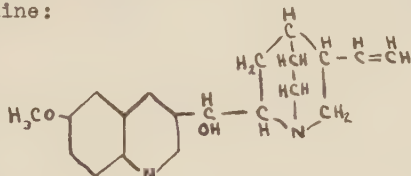
Fig. 10.

Discussion of results.--The rotations of quinine salts in chloroform have already been discussed and the "anomalous" rotations pointed out. When cellosolve is used as a solvent for the quinine salts the curves show less divergence. All acids except diphenic and 4,4'-dinitrodiphenic give approximately the same type of curve. The position of the substituents and the charges upon them do not seem to affect the rotation in any definite way.

With Betti's base nearly all acids give approximately a straight line. Diphenic and 4,4'-dinitrodiphenic again give a minimum although not a marked one. Phthalic acid gives abnormal results for both Betti's and Howard's base. Racemization probably takes place in these cases. Howard's base differs from Betti's base only in that it has a phenylethyl group in place of a phenyl group, yet with this substance all acids, including the diphenic acids give straight line curves.

The above results seem to indicate something peculiar in the behavior of both quinine and chloroform since, when cellosolve is substituted for chloroform, all acids except the diphenic acids fall into the same class, and when a simple base like Howard's base is substituted for quinine even these two acids behave like the others. Although the solvent plays a role in the observed rotation, the greatest disturbing factor is apparently the base. Morphine, a monoacid base, gives straight line curves for all acids. The fact that it has only one basic nitrogen atom does not account for this result since p-dimethylaminobenzal- β -naphtholphenylaminomethane also shows no abnormalities, even though the molecule contains two basic nitrogen atoms. The reduction product of the above compound, which has stronger basic properties, also produces no abnormalities. Here the rotation does not change with concentration of acid. Therefore, the cause

of the anomalous rotation of quinine with varying amounts of acid lies not in the two basic nitrogen atoms but in some other part of the molecule. The following structure is now generally accepted for quinine:



Hydroquinine, in which the vinyl group of quinine is reduced gives exactly the same sort of curves as quinine and therefore the vinyl group is not the cause of the anomaly. However, when acetyl- and benzoyl-quinine are used the minima disappear and the curves approach straight lines. The same is true of the curves for quininechloride. From these results it seems evident that the principal cause of the anomalous rotations of quinine salts is the secondary alcohol group. In what way this group influences the rotation is not clear. The fact that it is attached to an asymmetric carbon atom may have some influence, or the effect may possibly be due to the proximity of the alcoholic group to the quinoline nitrogen atom.

Experimental Part¹

Rotations of mixtures of 0.001 mols of quinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dcm. tube at 20° C.

0.001 mols of quinine, $\alpha_{5461}^{20^\circ} = -3.48^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
Acetic Acid		Chloroacetic Acid		Phenylpropionic Acid	
0.705	-2.92	0.445	-3.29	0.50	-2.90
1.08	2.96	0.765	2.73	0.90	2.54
1.18	3.28	1.13	2.60	1.00	2.49
2.07	5.21	1.62	3.38	1.10	2.79
2.64	5.98	2.22	4.45	1.50	3.68
5.58	7.83	3.24	5.87	2.00	4.84
8.16	8.33	7.92	8.46	3.00	6.09
15.45	8.82	18.74	9.01	5.00	6.91
18.43	9.07			10.00	7.22
glacial	8.44			20.00	7.19
Lauric Acid		Trichloroacetic Acid		Palmitic Acid	
0.518	-3.14	0.329	-3.43	1.00	-2.92
1.01	2.98	0.606	3.23	2.00	5.08
2.02	5.75	1.14	2.80	5.00	7.25
5.00	7.04	2.01	3.25	10.00	7.81
10.00	7.70	4.13	6.61	15.00	7.83
....		8.66	8.62		
Benzoic Acid		o-Phenylbenzoic Acid		o-Chlorobenzoic Acid	
0.50	-3.18	0.50	-3.32	0.512	-3.57
1.00	2.87	1.00	3.69	0.756	3.77
1.50	4.88	2.00	4.72	1.00	4.27
2.00	6.34			1.26	4.65
3.00	7.97			2.01	5.71
5.00	9.00			5.05	6.51
10.00	9.35			8.35	6.46
20.00	9.19				

¹D. W. Stanger co-operated in carrying out these experiments and a portion of his results are included here.

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
Phenylacetic Acid		Crotonic Acid		Cinnamic Acid	
0.50	-2.70	0.50	-2.91	0.10	-3.17
1.00	2.13	1.00	2.50	0.50	-1.15
2.00	4.26	1.50	3.80	0.70	-0.18
3.00	5.58	2.00	4.89	1.00	+1.47
5.00	6.37	3.00	6.21	1.30	+0.09
10.00	6.81	5.00	7.19	1.50	-0.92
20.00	6.88	8.00	7.61	2.00	2.68
....		10.00	7.76	3.00	4.38
....		20.00	7.82	5.00	5.40
....				7.00	5.70
....				10.00	5.75
....				20.00	5.47
Anisic Acid		o-Nitrobenzoic Acid		2,4-Dinitrobenzoic Acid	
0.50	-2.41	0.50	-1.05	0.25	-1.78
1.00	1.28	0.75	-0.13	0.50	+0.45
1.50	2.73	1.00	+1.31	0.65	+2.25
2.00	4.47	1.50	+0.66	0.75	+4.35
2.50	5.43	2.00	-0.32	1.00	+6.39
3.00	6.62*	3.00	-2.33	1.50	+4.69
5.00	7.06*	5.00	-4.87	2.00	+2.46
....				2.50	+0.16
....				3.00	-1.64
o-Toluic Acid		m-Nitrobenzoic Acid		2,4,6-Trinitrobenzoic Acid	
0.50	-3.33	0.50	-1.78	0.25	-1.56
0.75	3.30	1.00	0.18	0.50	+0.99
1.00	3.45	1.50	2.04	0.60	+1.93
1.25	3.81	2.00	3.93	1.00	+6.47**
1.50	4.33	3.00	6.79		
2.00	5.01	5.00	8.80		
3.00	5.72				
5.00	6.24				
11.00	6.42				

*Twice observed reading for 0.0005 mol quantities.

**Trace undissolved.

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
p-Toluic Acid		p-Nitrobenzoic Acid		Salicylic Acid	
0.50	-2.44	0.50	-1.16	0.514	-3.72
1.00	1.22	1.00	+1.80	0.76	4.04
1.50	3.12	1.50	-0.45	1.00	4.22
2.00	4.80	2.00	-2.88*	1.25	4.67
3.00	6.68			2.07	6.26
5.00	7.92			3.74	8.74
....				5.00	9.43
Anthranilic Acid		o-Iodobenzoic Acid		3,5-Dinitrobenzoic Acid	
0.50	-4.16	0.50	-3.77	0.50	+0.18
1.00	5.31	1.00	4.83	1.00	2.22
1.50	6.36	1.54	5.86	1.50	0.47
2.00	7.37	1.95	6.32		
3.20	8.35				
5.00	9.33				

*Trace undissolved.

Rotations of mixtures of 0.00025 mols of quinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dcm. tube at 20° C.

0.00025 mols of quinine, α 20°
5461 = -0.81°

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
Oxalic Acid		Phthalic Acid		Malonic Acid	
0.25	-0.29	0.25	-1.07	0.25	-0.94
0.50	+0.44	0.50	1.18	0.50	0.99
0.75	+0.09	0.75	0.99	0.75	0.95
....				1.00	0.95

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
Diphenic Acid		Maleic Acid		4-Nitrodiphenic Acid	
0.25	+0.50	0.26	-1.03	0.25	+0.17
0.50	1.38	0.50	1.06	0.50	0.95
0.75	0.56	0.75	1.06	0.75	1.34
1.00	0.19	1.08	1.10	1.00	1.69
1.25	-0.02			1.25	1.73
1.50	-0.12				
Adipic Acid		4,4'-Dinitrodiphenic Acid		Azelaic Acid	
0.25	-0.72	0.25	+0.11	0.254	-1.07
0.50	0.62	0.50	1.10	0.512	1.49
0.75	1.02	0.75	1.95		
1.00	1.28	1.00	2.33		
Sebacic Acid					
		0.25	-1.02		
		0.50	1.20		
		0.754	1.33		
		1.00	1.45		

Rotations of mixtures of 0.0000625 mols of quinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dcm. tube at 20° C.

0.0000625 mols of quinine, $\alpha_{5461}^{20^\circ} = -0.21^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
4,4'-Dinitrodiphenic Acid	
0.25	+ 0.01
0.50	0.27
0.75	0.45
1.00	0.68
1.25	0.54*
1.50	0.53**

*Trace undissolved.

**Undissolved part was filtered off.

Rotations of mixtures of 0.001 mols of quinine and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dcm. tube at 20° C.

0.001 mols of quinine, $\alpha_{5461}^{20^\circ} = -5.41^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
p-Nitrobenzoic Acid		Salicylic Acid		Phthalic Acid	
0.50	-6.17	0.50	-5.98	0.25	-5.57
1.00	6.83	1.00	6.67	0.50	5.85
1.50	6.93	1.50	6.65	0.75	6.03
2.00	6.94	2.00	6.68	1.00	6.14
3.00	6.88	3.00	6.68	2.00	6.23
5.00	6.75	5.00	6.63		

Mols Acid Mols Base	α $^{20^{\circ}}$ 5461
--	--

Glycollic Acid

0.46	-5.40
1.24	5.87
2.20	5.89
3.80	5.91
5.61	5.89

Rotations of mixtures of 0.00025 mols of quinine and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dcm. tube at 20° C.

0.00025 mols of quinine, α $^{20^{\circ}}$ $_{5461} = -1.37^{\circ}$

Mols Acid Mols Base	α $^{20^{\circ}}$ 5461	Mols Acid Mols Base	α $^{20^{\circ}}$ 5461	Mols Acid Mols Base	α $^{20^{\circ}}$ 5461
o-Nitrobenzoic Acid		o-Chlorobenzoic Acid		Oxalic Acid	
0.50	-1.53	0.50	-1.46	0.25	-1.39
1.00	1.71	1.00	1.51	0.50	1.31
2.00	1.70	2.00	1.54	0.75	1.28
5.00	1.75	5.00	1.54	1.50	1.25
Malonic Acid		Adipic Acid		Diphenic Acid	
0.25	-1.42	0.25	-1.40	0.25	-0.51
0.50	1.41	0.50	1.43	0.50	0.15
0.75	1.46	0.75	1.41	0.75	0.36
1.00	1.47			1.00	0.43
....				1.50	0.65
....				3.00	0.97

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
o-Phenylbenzoic Acid		3,3'-Dicarboxydiphenyl Acid		4,4'-Dinitro- diphenic Acid	
0.25	-1.30	0.25	-1.55	0.25	-0.41
0.50	1.28	0.50	1.63	0.50	+0.55
1.00	1.23	0.75	1.78	0.75	0.50
1.50	1.19	1.00	1.82	1.00	0.45
....				1.50	0.29
....				3.00	0.09
Phthalic Acid					
		0.25	-1.40		
		0.50	1.51		
		1.00	1.51		
		2.50	1.57		

Rotations of mixtures of 0.001 mols of hydroquinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dcm. tube at 20° C.

0.001 mols of hydroquinine, α 20°
5461 = -2.92°

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
Benzoic Acid		Diphenic Acid	
1.00	-1.63	0.50	+4.51
2.00	3.66	1.00	1.49
3.00	5.96		

Rotations of mixtures of 0.001 mols of acetylquinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dcm. tube at 20° C.

0.001 mols of acetylquinine, $\alpha_{5461}^{20^\circ} = -1.01^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
Benzoic Acid		o-Nitrobenzoic Acid		2,4-Dinitrobenzoic Acid	
1.00	-0.43	1.00	-0.96	-1.00	-1.77
2.00	0.31	2.00	1.06	2.00	1.70*
5.00	0.15	3.00	0.94		
Diphenic Acid		o-Chlorobenzoic Acid		Malonic Acid	
0.50	-1.51	1.00	-0.52	0.50	-1.13
0.67	1.68				
1.00	2.03				
Maleic Acid					
0.50			-1.53		

*Twice observed value for a 1 dcm. tube.

Rotations of mixtures of 0.001 mols of benzoylquinine and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20° C.

$$0.001 \text{ mols of benzoylquinine, } \alpha_{5461}^{20^\circ} = +4.88^\circ$$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
Benzoic Acid		o-Chlorobenzoic Acid		o-Nitrobenzoic Acid	
1.00	+5.30	1.00	+5.91	0.50	+5.23
2.00	5.51	2.00	6.04	1.00	5.49
5.00	5.72	5.00	5.54	2.00	5.66
....				3.00	5.98
....				5.00	6.35
2,4-Dinitrobenzoic Acid		Diphenic Acid		4,4'-Dinitrodiphenic Acid	
0.50	+4.01	0.25	+5.24	0.25	+1.27*
1.00	3.25	0.50	5.62	0.50	1.33*
2.00	3.49	1.00	6.26	1.00	1.56*

*Values obtained using 0.00025 mols of base.

Rotations of mixtures of 0.001 mols of quininechloride and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dm. tube at 20° C.

$$0.001 \text{ mols of quininechloride, } \alpha_{5461}^{20^\circ} = +2.17^\circ$$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
Benzoic Acid		o-Chlorobenzoic Acid		o-Nitrobenzoic Acid	
1.00	+1.88	1.00	+1.75	0.50	+2.11
2.00	1.69	2.00	1.22	1.00	1.78
5.00	1.50			2.00	0.68
....				3.00	-0.38

Mols Acid Mols Base	α ^{20°} 5461	Mols Acid Mols Base	α ^{20°} 5461	Mols Acid Mols Base	α ^{20°} 5461
2,4-Dinitrobenzoic Acid		Diphenic Acid		4,4'-Dinitrodiphenic Acid	
1.00	+1.23	0.50	+2.58	0.50	+0.62*
....		1.00	2.35	1.00	0.82*

*Values obtained using 0.00025 mols of base.

Rotations of mixtures of 0.00025 mols of morphine and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dm. tube at 20° C.

0.00025 mols of morphine, α ^{20°}₅₄₆₁ = -0.94°

Mols Acid Mols Base	α ^{20°} 5461	Mols Acid Mols Base	α ^{20°} 5461	Mols Acid Mols Base	α ^{20°} 5461
o-Chlorobenzoic Acid		o-Nitrobenzoic Acid		Phthalic Acid	
0.50	-0.87	0.50	-0.76	0.25	-0.91
1.00	0.82	1.00	0.65	0.50	0.85
2.00	0.69	2.00	0.63	1.00	0.81
5.00	0.71	5.00	0.61	2.50	0.80
Diphenic Acid			4,4'-Dinitrodiphenic Acid		
0.25	-0.88			0.25	-0.86
0.50	0.91			0.50	0.82
1.00	0.84			1.00	0.79
2.50	0.82			2.50	0.72

Rotations of mixtures of 0.001 mols of brucine and varying amounts of acid dissolved in 25 cc. of chloroform and taken in a 2 dcm. tube at 20° C.

0.001 mols of brucine, $\alpha_{5461}^{20^\circ} = -4.72^\circ$

$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$
Benzoic Acid		o-Chlorobenzoic Acid		Diphenic Acid	
1.00	-1.47	1.00	-1.76	0.50	-2.28
2.00	0.71	2.00	1.29	1.00	-0.04
3.00	0.61	3.00	1.10	1.50	+0.45
5.00	0.51	5.00	1.11		

Rotations of mixtures of 0.0005 mols of d-Howard's base and varying amounts of acid dissolved in 25 cc. of cellosolve and taken in a 2 dcm. tube at 20° C.

0.0005 mols of d-Howard's base, $\alpha_{5461}^{20^\circ} = +0.68^\circ$

$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$	$\frac{\text{Mols Acid}}{\text{Mols Base}}$	$\alpha_{5461}^{20^\circ}$
Acetic Acid		o-Nitrobenzoic Acid		Diphenic Acid	
0.74	+0.43	0.50	+0.24	0.25	+0.39
1.12	0.42	1.00	-0.02	0.50	0.29
1.51	0.31	2.00	-0.05	1.00	0.12
2.37	0.14	5.00	-0.07	2.50	0.10
8.74	-0.02				
glacial	-0.27				

Rotations of mixtures of 0.0005 mols of 1-Howard's base and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dcm. tube at 20° C.

0.0005 mols of 1-Howard's base, $\alpha_{5461}^{20^\circ} = -0.71^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
o-Nitrobenzoic Acid		o-Chlorobenzoic Acid	
0.50	-0.23	0.50	-0.32
1.00	+0.05	1.00	0.00
2.00	0.08	2.00	+0.08
5.00	0.08		
Phthalic Acid		4,4'-Dinitrodiphenic Acid	
0.25	-0.27	0.25	-0.20
0.50	0.10	0.50	+0.10
1.00	0.38	1.00	0.22
2.50	0.54	2.50	0.13

Rotations of mixtures of 0.000125 mols of p-Dimethylaminobenzal- β -naphthol-phenylaminomethane and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dcm. tube at 20° C.

0.000125 mols of p-Dimethylaminobenzal- β -naphthol-phenylaminomethane, $\alpha_{5461}^{20^\circ} = +2.77^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
o-Chlorobenzoic Acid		o-Nitrobenzoic Acid	
1.00	+2.85	1.00	+2.80
2.00	2.76	2.00	2.79
5.88	2.82		

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
Diphenic Acid		4,4'-Dinitrodiphenic Acid	
0.50 1.00	+2.81 2.85*	0.50	+2.83*

*Trace undissolved.

Rotations of mixtures of 0.00025 mols of p-Dimethylaminobenzyl- β -naphthol-phenylaminomethane and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dcm. tube at 20° C.

0.00025 mols of p-Dimethylaminobenzyl- β -naphthol-phenylaminomethane, α $\frac{20^\circ}{5461} = +1.97^\circ$

Mols Acid Mols Base	α 20° 5461	Mols Acid Mols Base	α 20° 5461
Benzoic Acid		o-Nitrobenzoic Acid	
0.50 1.00 2.00 5.00	+1.97 2.05 2.03 1.91	0.50 2.00 3.00 5.00	+1.57 2.03 1.78 1.96
Diphenic Acid		o-Chlorobenzoic Acid	
0.25 0.50 1.00	+1.92 1.62 1.59*	1.00 3.00	+1.99 2.01

*Trace undissolved.

Rotations of mixtures of 0.001 mols of d-Betti's base and varying amounts of acid dissolved in 25 cc. of cellosolve taken in a 2 dcm. tube at 20° C.

0.001 mols of d-Betti's base, $\alpha_{5461}^{20^\circ} = +2.66^\circ$

Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$	Mols Acid Mols Base	$\alpha_{5461}^{20^\circ}$
Acetic Acid		o-Chlorobenzoic Acid		o-Nitrobenzoic Acid	
1.21	+2.93	5.00	+2.70	1.00	+2.77
6.04	2.90			5.00	2.83
28.23	2.58				
43.98	2.37				
glacial	2.84				
m-Nitrobenzoic Acid		2,4-Dinitrobenzoic Acid		Adipic Acid	
3.50	+2.78	1.00	+2.76	0.50	+2.64
....		3.00	2.76	1.00	2.58
....				1.50	2.54
Sebacic Acid		Phthalic Acid		4,4'-Dinitrodiphenic Acid	
0.50	+2.95	1.50	+0.63	0.50	+2.30
2.50	2.89	4.00	0.64	1.50	2.54
Diphenic Acid					
			0.50	+2.58	
			2.50	2.89	

Rotations of mixtures of 0.0005 mols of d-Benzal- β -naphthol-phenylaminomethane and varying amounts of acid dissolved in 25 cc. of chloroform taken in a 2 dcm. tube at 20° C.

0.0005 mols of d-Benzal- β -naphthol-phenylaminomethane,
 $\alpha_{5461}^{20} = +2.75^{\circ}$

Mols Acid Mols Base	α_{5461}^{20}	Mols Acid Mols Base	α_{5461}^{20}	Mols Acid Mols Base	α_{5461}^{20}
o-Chlorobenzoic Acid		o-Nitrobenzoic Acid		Diphenic Acid	
1.00	+2.76	2.00	+2.75	0.50	+2.76*
2.00	2.75				

*Trace undissolved.

Acids.--To insure the purity of the acids used, those whose melting points deviated by two degrees or more from the accepted values were recrystallized until their melting points were brought within this limit of deviation. The following acids, not otherwise available, were prepared:

o-Phenylbenzoic acid was prepared from fluorenone according to the method of Graebe and Rateanu.¹ For further purification the acid was recrystallized from hot 40 per cent alcohol.

3,3'-Diphenyldicarboxylic acid was prepared from m-iodobenzoic acid methyl ester by the Ullmann synthesis.²

4-Nitrodiphenic acid was prepared from phenanthraquinone following Schmidt's³ method with some modifications suggested by

¹Graebe and Rateanu, Ann., 279, 260 (1894).

²Ullmann and Lowenthal, Ann., 332, 71 (1904).

³Schmidt, Ber., 36, 3731 (1903).

Werner's¹ directions for nitration. The mononitration was carried out by boiling 30 g. of phenanthraquinone dissolved in 350 cc. of nitric acid (sp. gr. 1.42) for twenty minutes. The 4-nitrodiphenic acid was obtained by the oxidation of the 2-nitrophenanthraquinone.

4,4'-Dinitrodiphenic acid was prepared by the oxidation of 2,7-dinitrophenanthraquinone which in turn was prepared by Schmidt and Kämpf's² method for the dinitration of phenanthraquinone. The acid was further purified by crystallization from boiling 30 per cent acetic acid.³

Bases.--The following bases were used and were prepared when not otherwise available:

Quinine, Mallinckrodt's anhydrous U.S.P., was used; m.p. 172° C.; $(\alpha)_{5461}^{20^{\circ}} = -134.2$ in chloroform for $c = 1.2968$.

Hydroquinine was prepared by the hydrogenation of quinine. About 0.3 g. of Raney's⁴ catalyst was added to 6.5 g. of quinine dissolved in dilute sulphuric acid and hydrogenation was started at three atmospheres pressure and continued for twelve minutes. The catalyst was separated by filtration and the filtrate made alkaline with sodium carbonate. The precipitated hydroquinine was dissolved in benzene, dry hydrogen chloride was passed into the solution and the precipitated hydrochloride, filtered and dried, melted at 232° C. The free base was liberated by dissolving the hydrochloride in water and treating with sodium carbonate. After drying for an hour at 100° C. it melted at 172° C. The hydroquinine thus obtained did not decolorize potassium permanganate, which proved the absence of quinine as an impurity.

¹Werner, Ann., 321, 336 (1902).

²Schmidt and Kämpf, Ber., 36, 3739 (1903).

³Schultz, Ann., 196, 26 (1879).

⁴Adkins and Covert, J. Am. Chem. Soc., 54, 1651 (1932).

$(\alpha)_D^{20} = -143.8^\circ$ for $c = 2.4$ g. in 95 per cent alcohol. The value given in the International Critical Tables¹ is $(\alpha)_D^{20} = -142.2^\circ$.

Acetylquinine was prepared by the action of acetic anhydride on quinine at 60-80° C. for several hours according to the directions of Hesse.² The product melted at 116-117° C. $(\alpha)_D^{20} = -27.0^\circ$ for $c = 1.4848$ g. in 95 per cent alcohol. The value given in the International Critical Tables³ is $(\alpha)_D^{14.4} = -30.9^\circ$ for $c = 1$ g. in 95 per cent alcohol.

Benzoylquinine was prepared according to the directions of Wunsch.⁴ The product so obtained melted at 129° C. and $(\alpha)_D^{20} = +119.3$ for $c = 1$ g. in absolute alcohol. Seekles⁵ gives a melting point of 138° C. and $(\alpha)_D^{19.2} = +119.9^\circ$.

Quininechloride was made according to the directions of Comstock and Königs⁶ except that quinine was used in place of quinine monohydrochloride; m.p. 151° C.; $(\alpha)_D^{15} = +59.1^\circ$ for $c = 1.966$ g. in absolute alcohol. The rotation obtained by Comstock and Königs was $(\alpha)_D^{15} = +61.0^\circ$.

Brucine, Eastman's practical, was purified by dissolving in chloroform and precipitating with dry ether. The precipitated brucine was dried at 100° C. for several hours; m.p. 178° C.; $(\alpha)_D^{20} = -120.5^\circ$ for $c = 1.5768$ g. in chloroform. Hilditch⁷ gives $(\alpha)_D^{20} = -121^\circ$ for $c = 2.5$ g. in chloroform.

¹"International Critical Tables," The McGraw Hill Book Co., New York, 1930, VII, 472.

²Hesse, Ann., 205, 315 (1880).

³Op. cit., p. 472.

⁴Wunsch, Ann. chim. (VII), 7, 126 (1896).

⁵Seekles, Rec. trav. chim., 42, 72 (1923).

⁶Comstock and Königs, Ber., 17, 1988 (1884).

⁷Hilditch, J. Chem. Soc., 93, 1388 (1908).

Morphine had a melting point of 252° C. and $(\alpha)_D^{23} = -131.1^\circ$ for c = 2.292 g. in absolute methyl alcohol. Schryver and Lees¹ give a melting point of 254° C. and $(\alpha)_D^{23} = -130.9^\circ$.

Betti's base (β -naphthol-phenylaminomethane) was prepared according to the directions of Marvel and Hiers.² The free base was resolved by fractional crystallization of the tartrate in alcoholic solution according to the directions of Betti.³ $(\alpha)_D^{20} = +59.75^\circ$ for c = 4.2664 g. in benzene. Betti gives $(\alpha)_D^{20} = +58.84^\circ$ under the same conditions.

d-Betti's Schiff base (d-benzal- β -naphthol-phenylaminomethane) was obtained by condensing d-Betti's base with benzaldehyde.⁴ $(\alpha)_D^{20} = +109.0^\circ$ for c = 0.7436 g. in benzene. Betti gives $(\alpha)_D^{20} = +110.68^\circ$.

d-p-Dimethylaminobenzal- β -naphthol-phenylaminomethane was prepared by condensation of p-dimethylaminobenzaldehyde with d-Betti's base; m.p. 220° C.; $(\alpha)_D^{20} = +694^\circ$ for c = 0.1900 g. in benzene. Betti⁵ gives $(\alpha)_D^{20} = +704.21^\circ$ in benzene.

d-p-Dimethylaminobenzyl- β -naphthol-phenylaminomethane was prepared by reduction of the Schiff base. 1.0 g. was suspended in 100 cc. of benzene and 0.3 g. of Raney's catalyst (washed first with alcohol and then with benzene) was added. Hydrogenation was started at three atmospheres and at the end of three hours the Schiff base was in solution and reduction was complete. The solution was filtered and the filtrate evaporated

¹Schryver and Lees, *ibid.*, 77, 1038 (1900).

²Marvel and Hiers, "Organic Syntheses," John Wiley and Sons, New York, 1932, Collective Vol. I, p. 372.

³Betti, *Gazz. chim. ital.*, 36, II, 392 (1906).

⁴*Ibid.*, 37, I, 62 (1907).

⁵*Ibid.*, 46, I, 200 (1916).

to dryness in a stream of air. The product recrystallized from alcohol had a melting point of 139-139.5° C. Two different reductions gave products with the following rotations: $(\alpha)_{5461}^{20^\circ} = +268.8^\circ$ and $+266.2^\circ$ for $c = 0.1816$ g. in dry ether.

The hydrochloride was prepared by passing dry hydrogen chloride into an ether solution of the reduced base; m.p. 175° C. (dec.).

Anal. Calcd. for $C_{26}H_{28}NOCl_2$: Cl, 15.58.

Found: Cl, 15.58 and 15.31 (Volhard).

Howard's base (β -naphthol- β -phenylethylaminomethane) was prepared according to the directions of Kharasch and Howard.¹

d- and l-Howard's base was prepared by resolving the racemic mixture. The free base, 16.0 g., was added to a hot solution of 10 g. of tartaric acid (theory 8.66 g.) in 150 cc. of alcohol. On further heating a clear solution was obtained, and then almost immediately the precipitate of the tartrate began to form. After standing overnight the precipitate was filtered off, boiled for a few minutes with 100 cc. of alcohol containing 1 g. of tartaric acid and cooled. The weight of the dry salt obtained was 10.14 g.; theory demands 12.33 g. The free base was liberated by treating the tartrate with dilute potassium hydroxide solution at 0° C. and extracting with ether. Five g. of crystalline d-base were obtained by evaporation of the dry ether extracts; m.p. 108 C. and $(\alpha)_{5461}^{20^\circ} = +187.5^\circ$ for $c = 1.1088$ g. in anhydrous ether.

On concentrating the combined alcohol filtrates by evaporating in a stream of air, successive portions of a solid salt separated until approximately 5 g. was obtained. The filtrate was now only 15 to 20 cc. in volume and quite syrupy. This was

¹Kharasch and Howard, J. Am. Chem. Soc., 56, 1371 (1934).

further evaporated in a stream of air until it solidified. On liberating the base from this mixture of salt and tartaric acid, drying the ether extract and crystallizing out the base, 4 g. of the 1-form were obtained. This gave a melting point of 108°C . and $(\alpha)_{5461}^{20^{\circ}} = -188.8^{\circ}$ for $c = 1.1088$ g. in anhydrous ether.

Solvents.--The following solvents were used and purified as described:

Chloroform, U.S.P., was washed five times with distilled water to remove the alcohol, dried over anhydrous calcium chloride and distilled. The constant boiling was tested before use by taking the rotation of 0.3242 g. of quinine dissolved in 25 cc. of the solvent, using a 2 dcm. polariscope tube. The chloroform was rejected if $\alpha_{5461}^{20^{\circ}}$ deviated more than 0.02° from -3.48° . Later the rotation of the mixture of 0.3242 g. of quinine and 0.1220 g. of benzoic acid was used as a test. For this solution $\alpha_{5461}^{20^{\circ}} = -2.87^{\circ}$.

Cellosolve (monoethyl ether of ethylene glycol), Union Carbide, was distilled to obtain a constant boiling fraction.

Summary

1. The Kuhn hypothesis has been shown to be invalid, since with quinine in chloroform solution the curve for 4,4'-dinitrodiphenic acid is not any more abnormal than those for several other acids which probably can not be dissymmetrized.

2. With quinine, the shape of the curves depends upon the type of acid used. For example, benzoic acids containing negative substituents in the ortho-position give a type of curve different from that produced by benzoic acids containing positive substituents in the same position. Para-substituted benzoic acids give curves of the latter type.

3. The solvent does not greatly affect the shape of the rotation curves of any salts, save those of quinine.

4. The vinyl group of quinine exerts only a negligible effect on the shape of the curves.

5. The principal cause of the abnormality of the curves for quinine is the secondary alcohol group.

6. All the other bases investigated, except quinine, give curves which are without a minimum and show no anomalies even in the cases of the substituted diphenic acids.

